United States Patent [19]

Lin et al.

[11] **Patent Number:**

6,028,183

Date of Patent: [45]

Feb. 22, 2000

[54] PYRIMIDINE DERIVATIVES AND OLIGONUCLEOTIDES CONTAINING SAME

- [75] Inventors: Kuei-Ying Lin, Fremont; Mark D. Matteucci, Portola Valley, both of Calif.
- Assignee: Gilead Sciences, Inc., Foster City, Calif.
- Appl. No.: 08/966,392 [21]
- Filed: Nov. 7, 1997
- Int. Cl.⁷ C07H 19/00; C07H 21/00 [51] [52] U.S. Cl. 536/22.1; 536/23.1; 536/25.3; 536/25.31; 536/25.32; 536/25.34; 536/25.4;
- 435/6; 435/87; 435/90; 544/249
- 536/25.3, 25.31, 25.32, 25.34, 25.4; 435/6, 87, 90; 544/249

[56] References Cited

U.S. PATENT DOCUMENTS

4,233,402	11/1980	Maggio et al
5,286,717	2/1994	Cohen et al
5,502,177	3/1996	Matteucci et al.
5,594,121	1/1997	Froehier et al
5,614,617	3/1997	Cook et al
5,614,622	3/1997	Iyer et al
5,623,068	4/1997	Reddy et al
5,645,985	7/1997	Froehler et al
5,668,272	9/1997	Prasad et al
5,728,528	3/1998	Mathies et al

FOREIGN PATENT DOCUMENTS

0 487 289 A2	5/1992	European Pat. Off
0 541 153 A1	5/1993	European Pat. Off
62-059293 A2	3/1987	Japan .
WO 88/10264	12/1988	WIPO .
WO 90/15065	12/1990	WIPO .
WO 91/06626	5/1991	WIPO .
WO 91/06629	5/1991	WIPO .
WO 92/02258	2/1992	WIPO .
WO 92/20702	11/1992	WIPO .
WO 93/10820	6/1993	WIPO .
WO 93/13121	7/1993	WIPO .
WO 93/24507	12/1993	WIPO .
WO 96/05298	2/1996	WIPO .
WO 96/37504	11/1996	WIPO .
WO 97/14706	4/1997	WIPO .
WO 97/28176	8/1997	WIPO .
WO 97/31008	8/1997	WIPO .
WO 97/32888	9/1997	WIPO .

OTHER PUBLICATIONS

Bell, et al., "Highly Effective Hydrogen-Bonding Receptors for Guanine Derivatives", 34(19):2163-2165, Angew Chem Int Ed, 1995.

Dande, et al., "Regioselective Effect of Zwitterionic DNA Substitutions on DNA Alkylation: Evidence for a Strong Side Chain Orientational Preference", 36:6024-6032, Bio-

Haginoya et al., "Nucleosides and Nucletides. 160, Synthe-Oligodeoxyribonucleotides sis 5-(N-Aminoalky)carbamoyl-2'-deoxyuridines by a New Postsynthetic Modification Method and Their Thermal Stability and Nuclease-Resistance Properties", 8:271-280, Bioconj Chem, 1997.

Lin et al., "Tricyclic 2'-Deoxycytidine Analogs: Synthesis and Incoporation into Oligodeoxynucleotides Which Have Enhance Binding to Complementary 117:3873-3874, J. Am Chem Soc, 1995.

Matteucci et al., "In pursuit of antisence", 384(7):20-22, Nature, 1996.

Prober et al., "A System for Rapid DNA Sequencing with Fluroescent Chain-Terminating Dideoxynucleotides", 238:336-341, Science, 1987.

"Effects al.. 5-(N-aminohexyl)carbamoyl-2'-dexyuridine on endonuclease stability and the ability of oligodeoxynucleotide to activate RNase H", 25(19):3777-3782, Nuc Acids Res,

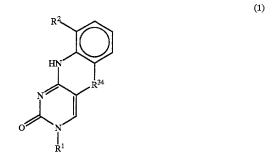
Ulmann et al, "Antisense Oligonucleotides: A New Therapeutic Principle", 90(4):543-584, Chem Rev, 1990.

Primary Examiner-James O. Wilson Attorney, Agent, or Firm—Woodcock Washburn Kurtz Mackiewicz & Norris LLP

[57]

ABSTRACT

Compounds having structure (1)



wherein R¹ is —H a protecting group, a linker or a binding partner; and R^2 and \hat{R}^{34} are as defined in the specification. The invention also provides intermediates and methods make the structure (1) compounds, as well as methods to use the compounds as labels in diagnostic assays and to enhance binding to complementary bases.

30 Claims, No Drawings